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(21) International Application Number: PCT/US98/13387 (22) International Filing Date: 26 June 1998 (26.06.98) (30) Priority Data: 08/883,656 27 June 1997 (27.06.97) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 08/883,656 (CIP) Filed on 27 June 1997 (27.06.97)		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIGO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).	
Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>			
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(54) Title: NEUROPROTECTIVE METHODS AND REAGENTS

(57) Abstract

One aspect of the present application relates to a method for limiting damage to neuronal cells by ischemic or epoxic conditions, e.g., such as may be manifest by a reduction in brain infarct volume, by administering to an individual a hedgehog therapeutic or ptc therapeutic in an amount effective for reducing cerebral infarct volume.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/13387

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K31/47

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 519 035 A (MAIESE KENNETH ET AL) 21 May 1996 see abstract see column 2, line 20-34; claims 1-5; examples 1,2 --- SATOH ET AL.: "Neuroprotective properties of a protein kinase inhibitor against Ischemia-induced neuronal damage in rats and gerbils" BRITISH JOURNAL OF PHARMACOLOGY, vol. 118, no. 7, 1996, pages 1592-1596, XP002092077 see abstract --- -/-/	1-12, 16-19, 21-28, 30-38
X		1-12, 16-19, 22-28, 30-38

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *S* document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 February 1999	18/02/1999
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer A. Jakobs

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/13387

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MAIESE ET AL.: "Protein Kinases Modulate the Sensitivity of Hippocampal Neurons to Nitric Oxide Toxicity and Anoxia" JOURNAL OF NEUROSCIENCE RESEARCH, vol. 36, no. 1, 1993, pages 77-87, XP002092078 see abstract see page 79, column 1, paragraph 1 - page 81, column 2, paragraph 2; figure 1 see page 83, column 2, paragraph 2 - page 84, column 1, paragraph 3 -----	1-12, 16-28, 30-38
X	PHILLIS ET AL.: "Mechanism of glutamate and aspartate release in the ischemic rat cerebral cortex" BRAIN RESEARCH, vol. 730, no. 1-2, 1996, pages 150-164, XP002092079 see abstract; figure 7; tables 2,3 -----	1-12, 16-28, 30-38
X	EP 0 187 371 A (ASAHI CHEMICAL IND ; HIDAKA HIROYOSHI (JP)) 16 July 1986 see abstract see page 2, line 1-10; example 4 see page 8, line 6 - page 14, line 4 -----	1-12, 16-19, 22-28, 30-38
P,X	WO 98 12326 A (CHUANG PAO TIEN ; HARVARD COLLEGE (US); MCMAHON ANDREW P (US)) 26 March 1998 see page 3, line 15 - page 9, line 10; claim 13 -----	1-14,40

INTERNATIONAL SEARCH REPORT

I. National application No.

PCT/US 98/ 13387

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 1-34, 40

because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 1-34, 40

are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

See FURTHER INFORMATION SHEET PCT/ISA/210

3. Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking(Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

In view of the large number of compounds, which are defined by the general definition(s)/formulae used in claims 1-20, 22-40, the search had to be restricted for economic reasons. The search was limited to the compounds for which pharmacological data was given and/or the compounds mentioned in the claims, and to the general idea underlying the application. (See Guidelines, chapter III, paragraph 2.3).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 98/13387

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 5519035	A	21-05-1996		NONE
EP 0187371	A	16-07-1986	JP 1795364 C	28-10-1993
		JP 5003851 B	18-01-1993	
		JP 61227581 A	09-10-1986	
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		JP 4081986 B	25-12-1992	
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WO 9812326	A	26-03-1998	AU 4489297 A	14-04-1998